REMARKS

Claims 11-20 and 27-36 were pending in the application upon the issuance of the Final Office Action dated October 12, 2006. In the present amendment, claims 11, 15 and 17 have been amended, claims 28-29, 31-32 and 34-45 have been have been cancelled, and new claims 37-48 have been added. Support for these amendments may be found throughout the specification and claims as originally filed. *Accordingly, no new matter has been added.*

Upon entry of the foregoing amendments, claims 11-20, 27, 30, 33 and 36-48 will be pending and under examination. The claim cancellations requested herein should in no way be construed as acquiescence to any of the rejections and have been made solely to expedite prosecution of the application. Applicants reserve the right to pursue the claims as originally filed and/or prior to amendment herein in this or a separate application(s).

Examiner Interview

Applicants gratefully thank the Examiner for the courtesy of the telephonic interviews held between the Examiner and Applicants' attorney on April 23, 2007. During the interview, the enablement and written description rejections of claims 11-20 and 27-36 were discussed, and various claim amendments were suggested to the Examiner. However, agreement was not reached. The substance of the interview is incorporated in the remarks set forth below.

Claims-Objections

The claim set was objected to for "not beginning with a sentence of which the claims are an object." Accordingly, the claim set has been amended to begin with the phrase "We claim," as suggested by the Examiner.

The claims were also objected to for a number of inadvertent typographical errors which have been corrected by the foregoing amendments to the claims.

Claim Rejections – 35 USC § 112-Second Paragraph

Claims 32 and 35 were rejected as indefinite on the ground that the phrase "wherein the ribosome-inactivating protein an amino acid sequence." Applicants respectfully submit that this rejection has been rendered moot by the cancellation of claims 32 and 35.

Claim Rejections – 35 USC §112 - First Paragraph

Enablement

The rejection of claims 11-20 for lack of enablement was maintained, and further applied to new claims 27-36. Specifically, the Office Action states:

> The specification fails to teach the active, full-length protein or the active site residue or any polynucleotide encoding such. ....While it is acknowledged that techniques for making fusion proteins, making and expressing polynucleotides, testing polypeptides for ribosome-inactivating activity are standard in the art, to make and test the full-scope of the recited polynucleotides for encoding polypeptides having ribosome-inactivating activity, with no guidance as to the relationship between the structure of a polypeptide and the function of ribosome-inactivating activity, clearly represents undue experimentation. (Office Action at page 4)

Applicants respectfully traverse this rejection as applied to the pending claims.

The test for enablement is whether one skilled in the art could make or use the claimed invention from the disclosure in the patent application with information known in the art without undue experimentation. *United States v. Telectronics, Inc.*, 857 F.2d 778, 785 (Fed. Cir.1988). The specification *need not contain an example* if the invention is otherwise disclosed in such manner that one skilled in the art will be able to practice it without an undue amount of experimentation. *In re Borkowski,* 422 F.2d 904, 908 (CCPA 1970) (emphasis added)

Applicants respectfully submit that disclosure *a priori* of the full-length amino acid sequence and corresponding nucleic acid coding sequence of bouganin RIP is not required to meet the requirements of enablement for the claims as presently amended. The skilled artisan provided with the information in the application and publicly available information would understand how to make and use the invention without undue experimentation.

Applicants specification discloses the isolation of a novel, purified type-1 ribosome inactivating protein, bouganin RIP (see page 10, Example 1) with a *functional activity* (capable of inhibiting protein synthesis), and immunotoxin conjugates containing this novel RIP (see page 15, Example 6) which demonstrate lower cytotoxicity than other type-1 RIPs (*e.g.*, see page 19, lines 1-4). The specification further provides specific *structural information* for approximately 60% of the N-terminal amino acid sequence for the mature protein (SEQ ID NO:9), the

nucleotide sequence encoding this amino acid sequence (SEQ ID NO:8), and provides methods for obtaining the remaining nucleic acid sequences using routine procedures well-known to those skilled in the art.

Indeed, it is noted that Hartog *et al.*, which disclose the cloning of the complete nucleotide and amino acid sequences of bouganin, followed the teachings of the specification (see, *e.g.*, page 1773 "Cloning of bouganin"). They used the same source (*B. spectabills* Wild leaves) to prepare bouganin RNA, and the same primers to amplify the bouganin cDNA (Note: primers 1-3, 5 and 6 listed in Table 1 of Hartog *et al.* are the same as the PCR primers set forth in Example 8 of the instant specification). They also used the same 360 bp PCR product disclosed by Applicants to obtain the complete nucleotide and amino acid sequences using only routine procedures. Accordingly, Hartog *et al.* effectively demonstrates that the specification is sufficiently enabling for the skilled artisan to make and use the claimed invention.

Furthermore, the aforementioned functional and structural information provided in the specification clearly demonstrate that Applicants were in possession of a novel member of a protein family with common structural and functional characteristics known to those skilled in the art. For example, at the time of Applicants' invention, it was known that Type 1 ribosome-inactivating proteins have a common N-glycosidase activity (ribosome inhibiting activity), a basic isoelectric point and a mass of 26-30 kDa. In addition, publicly available sequence alignments of a number of ribosome inactivating proteins had shown that there are invariant or highly conserved amino acid residues particularly in the active site (e.g., see Hartog *et al.*, at page 1776, citing Kim *et al., Prot. Eng.* 5:775, 779, 1992; and Hung *et al., Eur. J. Biochem.* 219:83-87, 1994).

Accordingly, one of ordinary skill in the art provided with the teachings of the specification and publicly available knowledge pertaining to the common structural and functional characteristics of various members ribosome-inactivating protein family would not have required the disclosure of a specific full-length amino acid or nucleotide sequence in the specification in order to understand how to make and use the claimed invention without undue experimentation.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of this rejection.

Written Description

The rejection of claims 11-20 for lack of adequate written description was maintained, and further applied to new claims 27-36 on the ground that the skilled artisan would not reasonably conclude that the inventors were in possession of the claimed invention because the specification fails to disclose any polynucleotide encoding any polypeptide having ribosome-inactivating activity. Applicants respectfully traverse this rejection as it pertains to the pending claims.

The correct standard for written description does not require a specification disclose each and every embodiment encompassed by a claim, but that the specification provides sufficient disclosure for one skilled in the art at the time of the invention to make and use the embodiments encompassed by the claims without undue experimentation. For example, as the Federal Circuit explained in *Lizardtech v. Earth Resource Mapping, Inc.* 424 F. 3d 1336 (Fed. Cir. 2005)

> [a] claim will not be invalidated on section 112 grounds simply because the embodiments of the specification do not contain examples explicitly covering the full scope of the claim language. *See* Union Oil Co. v. Atl. Richfield Co., 208 F.3d 989, 997 (Fed. Cir. 2000). That is because the patent specification is written for a person of skill in the art, and such a person comes to the patent with the knowledge of what has come before. In re GPAC Inc., 57 F.3d 1573, 1579 (Fed. Cir. 1995). Placed in that context, it is unnecessary to spell out every detail of the invention in the specification; only enough must be included to convince a person of skill in the art that the inventor possessed the invention and to enable such a person to make and use the invention without undue experimentation

The claims as amended specify that the claimed nucleic acid encode a ribosome-inactivating protein comprises an amino acid sequence at least 75% identical to SEQ ID NO:9, and/or comprise the nucleotide sequence set forth in SEQ ID NO:8. These sequences correspond, respectively, to 60% of the amino acid sequence of the mature protein and open reading frame of the nucleic acid encoding the protein. The instant specification further provides an alignment of the N-terminal amino acid sequence set forth in SEQ ID No. 1 with 15 other known type-1 RIPs, describes methods for generating and expressing the claimed polynucleotides, and discloses methods for testing the encoded polypeptides for ribosome-inactivating activity.

Accordingly, Applicants respectfully submit that the skilled artisan presented with the teachings of Applicants' specification along with the disclosure in professional publications of the amino acid and nucleotide sequences of other known RIPs including detailed information of the invariant and conserved amino acids contained within the active site would conclude that Applicants were in possession of the invention as presently claimed. In a recent Federal Circuit decision, the court held that,

> (1) examples are not necessary to support the adequacy of written description (2) the written description standard may be met (as it is here) even when actual reduction to practice of an invention is absent; and (3) there is no per se rule that an adequate written description of an invention that involves a biological macromolecule must contain a recitation of known structure. *Falkner et al. v. Inglis et al.*, 448 F.3d 1357 (U.S. App. 2006)

In view of the foregoing, reconsideration and withdrawal of this rejection is respectfully requested.

New Matter

Claims 29, 32 and 35 were rejected on the ground that the specification fails to teach the limitation of a polynucleotide encoding a protein comprising or consisting of a polypeptide having at least 75% homology to SEQ ID NO:9.

Claims 29, 32 and 35 have been cancelled without prejudice. However, Applicants respectfully traverse this rejection as it pertains to the pending claims. Support for the term "75% homology" may be found in claims 1-5 as originally filed. Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

CONCLUSION

In view of the remarks set forth above, it is respectfully submitted that this application is in condition for allowance. If there are any remaining issues or the Examiner believes that a telephone conversation with Applicants' Attorney would be helpful in expediting prosecution of this application, the Examiner is invited to call the undersigned at (617) 227-7400.

Applicants believe that no fee is due with the filing of this paper, however, should any fee be due, the Director is authorized to charge it to the Deposit Account No. 12-0080, under PNJ-005CN, from which the undersigned is authorized to draw.

Dated: August 9, 2007

Respectfully submitted,

By _____

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